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Oral Medicine

Lack of evidence of hepatic disease in patients with oral lichen planus in Serbia

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OBJECTIVE: The reported frequency of chronic liver disease, and particularly, Hepatitis C virus (HCV) infection in patients with oral lichen planus (OLP) shows geographical variation. The aim of this study was to determine the prevalence of chronic hepatic disease, Hepatitis B virus and HCV infection in patients with OLP and control subjects resident in Serbia.

PATIENTS AND METHODS: In this prospective study 48 patients with OLP (33 women and 15 men, with a mean age of 49.7 years) and 60 control subjects (38 women and 22 men, with a mean age of 46.7 years) were examined for the presence of serological evidence of chronic hepatic disease, Hepatitis B surface antigen (HBsAg) and anti-HCV seropositivity.

RESULTS: All patients with OLP had normal liver function. HBsAg was not found in any of the patients with OLP or control group. None of the patients with OLP or control subjects were HCV seropositive.

CONCLUSION: Patients with OLP resident in Serbia do not have evidence of chronic liver disease or infection with HBV or HCV. The exact aetiological role between hepatic disease and OLP remains unclear.
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Keywords: oral lichen planus; hepatitis C virus; hepatitis C infection; anti-HCV; HBsAg

Introduction

An association between lichen planus (LP) and chronic active hepatitis (CAH) was first reported by Rebora *et al* (1978). Later studies found an increased prevalence of CAH in patients with LP ranging from 4.0 to 13.5% (Rebora *et al*, 1982; Korkij *et al*, 1984; Rebora and Rongioletti, 1984; Ayala *et al*, 1986; Cottoni *et al*, 1988; del Olmo *et al*, 1989; Gandolfo *et al*, 1992). In addition, in two studies of LP patients from Italy and Spain an increased frequency of hepatic cirrhosis was noted [del Olmo *et al*, 1989; Gruppo Italiano Studi Epidemiologici in Dermatologia (GISED), 1990]. In contrast, some authors have been unable to demonstrate any strong association between oral lichen planus (OLP) and hepatic disease (Scully *et al*, 1985; El-Kabir *et al*, 1993).

In the last 10 years a number of studies have investigated the relationship between HCV infection and LP. A significant high prevalence of ant-HCV antibodies in patients with OLP has been found in patients group from Southern Europe, Japan, The USA, Brazil, Thailand and Pakistan (Divano *et al*, 1992; Rebora *et al*, 1992; Bagan *et al*, 1994; Gandolfo *et al*, 1994; Santander *et al*, 1994; Nagao *et al*, 1995; Tanei *et al*, 1995; Carrozzo *et al*, 1996; Sanchez-Perez *et al*, 1996; Bagan *et al*, 1998; Mignogna *et al*, 1998; Chuang *et al*, 1999; Beaird *et al*, 2001; Chainani-Wu *et al*, 2001; Figueiredo *et al*, 2002; Klanrit *et al*, 2003; Mahboob *et al*, 2003). However, a significant association between HCV and OLP has not been confirmed by studies from the UK (Ingafou *et al*, 1998), France (Cribier *et al*, 1994; Chosidow *et al*, 1997), The Netherlands (van der Meij and van der Waal, 2000), Nepal (Garg *et al*, 2002) and Nigeria (Daramola *et al*, 2002). However, different results of the association between HCV and LP were reported in two studies from Germany (Imhof *et al*, 1997; Grote *et al*, 1998). It has been suggested that discrepancies observed between studies from different countries could reflect the varying geographic distribution of HCV infection between countries, a selection bias of the population studied, or a genetic predisposition in relation to immune responsiveness (Roy and Bagg, 1999).

The incidence of chronic HCV infection in Serbia (central part of Serbia and Vojvodina) in 2002 was 1.76/100 000 inhabitants, compared with 0.78/100 000 inhabitants in 2001 and 0.70/100 000 inhabitants in 2000. The incidence of chronic HBV infection in Serbia was 0.58/100 000 inhabitants in 2000, 0.59/100 000 inhabitants in 2001 and then increased remarkably in 2002 when it was 1.64/100 000 inhabitants (Institute for Health Care, Serbia, 2003).

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The aim of this study was to determine the frequency of HCV-antibodies in patients with OLP and compare it to that of control subjects.

Patients and methods

Forty eight consecutive patients (33 women, 15 men) with OLP, who attended the Oral Medicine Section of the Department of Stomatology, Faculty of Medicine, Novi Sad, Serbia between January 2002 and February 2004, were included in the study. The diagnosis of OLP was based upon both clinical and histological findings (WHO Collaborating Centre for Oral Precancerous Lesions, 1978). The average age was 49.7 years. Seven patients had both oral and cutaneous lesions and 41 had only oral lesions with multiple site involvement and symmetrical distribution. Among the 48 patients studies, 25 had erosive and ulcerative lesions, 20 had reticular lesions, two had plaque-like lesions and one had bullous lesions. The control group consisted of 60 individuals seeking dental treatment at our school. None had oral lesions including OLP. There were 38 women and 22 men, with a group mean age of 46.7 years.

All patients and control subjects were asked about their potential risk of viral hepatitis and resultant hepatic disease (previous receipt of blood transfusion, injecting drug use, tattooing and high risk sexual activities.

Hepatic function was estimated with serum levels of total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase using standard laboratory methods.

All serum samples of the patients and the controls were tested for hepatitis B surface antigen (HBsAg) by enzyme-linked immunosorbent assay (ELISA) (Organon Teknika, The Netherlands). Testing for antibody to HCV was performed by ELISA (UBI HCV EIA 4.0; United Biologicals Inc., New York, NY, USA) in both groups.

Student's *t*-test was used to evaluate the statistical differences of the means between the two groups, and chi-square test with Yates' correction to compare relative frequencies. *P*-values lower than 0.05 were considered statistically significant.

Results

The demography, risk factors for liver disease, and laboratory results of the patients with OLP and of the controls, are shown in Table 1.

No difference was found between the OLP and the control groups, regarding the mean age, sex, surgical treatments, blood transfusions and alcohol consumption. None of the patients with OLP or control subjects had any other risk factors for liver diseases.

There were no biochemical features of chronic hepatic disease in the patients with OLP or control subjects. In addition, there were no significant differences in the hepatic serological markers between the two groups.

The HBsAg was not found in any of the patients with OLP or control group. None of the patients with OLP or control subjects were HCV seropositive.

Discussion

Although no definitive relationship between liver disease and LP may be established there is a suggestion that in the presence of LP the performance of liver function tests is advisable (Epstein, 1984; Bagan *et al*, 1994; Mignogna *et al*, 1998, 2000). The present study shows that observed mean value for total bilirubin was within normal limits in the group of patients with OLP. Furthermore, the liver enzymes values (ALT, AST, ALP) did not reflect any abnormal response to liver function tests in patients with OLP. Thus the present findings are in agreement with those from previous similar reports (El-Kabir *et al*, 1993; Ingafou *et al*, 1998).

Some previous studies have found a tendency for patients with erosive OLP to have chronic hepatic disease (Ayala *et al*, 1986; Cottoni *et al*, 1988; Bagan *et al*, 1992) but this was not observed in the present study. Bagan *et al* (1994) suggested that liver disease might increase the tendency to aggressive oral lesion of LP.

An association between LP and hepatitis B virus (HBV) infection has been suggested as HBsAg-positive developing LP compared with HBsAg-negative patients (GISED, 1990). In addition, there are reports of mainly

Table 1 Features of patients with oral lichen planus and controls

Features	*OLP* ($n = 48$)	*Controls* ($n = 60$)	*Statistical significance*
Age (years; mean ± s.d.)	49.7 ± 10.5	46.7 ± 8.9	NS
Sex (male/female)	15/33	22/38	NS
Surgical treatments	5	6	NS
Blood transfusions	1	0	NS
Alcohol consumption			
Occasional	6	9	NS
Every day	0	0	
Total bilirubin (μmol l^{-1}; mean ± s.d.)	9.2 ± 2.4	8.4 ± 2.3	NS
ALT (U l^{-1}; mean ± s.d.)	21.0 ± 9.0	19.0 ± 7.5	NS
AST (U l^{-1}; mean ± s.d.)	19.6 ± 6.3	17.6 ± 5.4	NS
ALP (U l^{-1}; mean ± s.d.)	72.0 ± 26.2	65.8 ± 21.7	NS
HBsAg	0	0	
Anti-HCV	0	0	

NS = not significant.

skin lichenoid eruption following administration of different HBV vaccines (Aubin, 1994; Rebora *et al*, 1999). The present study did not find any such association and previous work involving a more limited number of patients than the present study have also not observed such an association (del Olmo *et al*, 1990; Carrozzo *et al*, 1996; Garg *et al*, 2002). Bagan *et al* (1994) reported that HBsAg was positive in four of the 40 patients with LP with altered levels of liver enzymes, whereas Sanchez-Perez *et al* (1996) found HBsAg in one of 78 patients with LP and in two of 82 controls. Recently, in a study of 60 OLP patients and 60 control subjects no differences was found between the OLP and the control groups, regarding the prevalence of single HBV marker and increased ALT (Klanrit *et al*, 2003).

The primary purpose of this prospective study was to determine the frequency of anti-HCV antibodies in patients with OLP and control subjects. Although the present study involved limited number of patients, none of the patients with OLP or control subjects were HCV seropositive. This observation is in accordance with the findings of some other studies (Ingafou *et al*, 1998; Tucker and Coulson, 1999; van der Meij and van der Waal, 2000; Garg *et al*, 2002). Interestingly, more frequent anti-HCV positivity in the groups of OLP with chronic liver disease (CLD) (78%) and CLD (42.8%) than in the OLP group (3.1%) might suggest that HCV infection plays an aetiopathogenic role in CLD associated with OLP, whereas the majority of patients suffering exclusively from OLP are not infected by HCV (del Olmo *et al*, 2000). As previously mentioned, 52% of cases in this study had erosive lesions, whereas in 41.8% of patients the lesions were exclusively reticular, and none of these patients with OLP had serological evidence of HCV infection. In contrast, a statistically significant association has previously been observed between erosive OLP and HCV infection (Carrozzo *et al*, 1996; Sanchez-Perez *et al*, 1996; Dupond *et al*, 1998; Gimenez-Garcia and Perez-Castrillon, 2003). Very recently, Klanrit *et al* (2003) found five patients (8.33%) with OLP infected with HCV and all of them had atrophic-erosive form. The same study could not clarify the distribution of the form of OLP in patients with HCV infection because they had only six (10%) patients with reticular lesions. On the contrary, Bagan *et al* (1998) found the 17 patients with HCV infection who manifested OLP exhibited a marked tendency to have only reticular lesions (70.6%). Likewise, they found that 23 of 100 OLP patients had HCV infection and 73.92% of them presented with atrophic-erosive lesions. Recently, Mignogna *et al*, (2000) found that the reticular form was more frequent in HCV-positive patients, whereas plaque lesions were more prevalent in HCV-negative patients. There were no significant differences between both groups when erosive and atrophic OLP lesions were considered. Moreover, Romero *et al* (2002) reported that reticular OLP was the most frequent clinical presentation in both HCV-positive (57.1%) and HCV-negative patients (63.6%). Also, no statistically significant differences could be established in terms of density of subepithelial inflammatory infiltrate between the groups. Furthermore, Nagao *et al* (2000) reported no significant differences in the histopathological characteristics of idiopathic and HCV-associated OLP. Carrozzo *et al* (2001) suggested that HCV-related OLP appears to be associated with the HLA-DR6 allele and this could partially explain the peculiar geographic heterogeneity of the association between HCV and LP.

In conclusion, the present data indicate that patients with OLP resident in Serbia do not have an increased frequency of hepatic disease or evidence of HBV or HCV infection. These findings suggest that HCV infection in OLP patients in the Province of Vojvodina, Serbia is not common and further suggest that any association between HCV and OLP is inconsistent and possibly influenced by the geographic distribution of HCV disease and/or genetically based factors.

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